



# Exploration of the Role of Gastroesophageal Reflux Disease in Chronic Obstructive Pulmonary Disease Patients – A Nationwide Population Based Cohort Study

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## Introduction

The underlying causes of 25%~35% of chronic obstructive pulmonary disease (COPD) cases of severe exacerbation cannot be identified. The prevalence of gastroesophageal reflux disease (GERD) among COPD patients is significantly higher than that of the normal population. This study aimed to investigated whether GERD is associated with an increased risk of COPD exacerbation requiring hospitalization or admittance to an emergency department by analyzing a nationwide healthcare database.

## Material and Methods

This study employed a population-based retrospective cohort design to analyze the data of 1,976 COPD subjects with GERD as an exposure cohort and 3,936 COPD subjects without GERD as a comparison group. We individually tracked each subject in this study for 12 months and identified those subjects who experienced an episode of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Hazard ratios (HR) were calculated using Cox proportional hazards regression analysis.

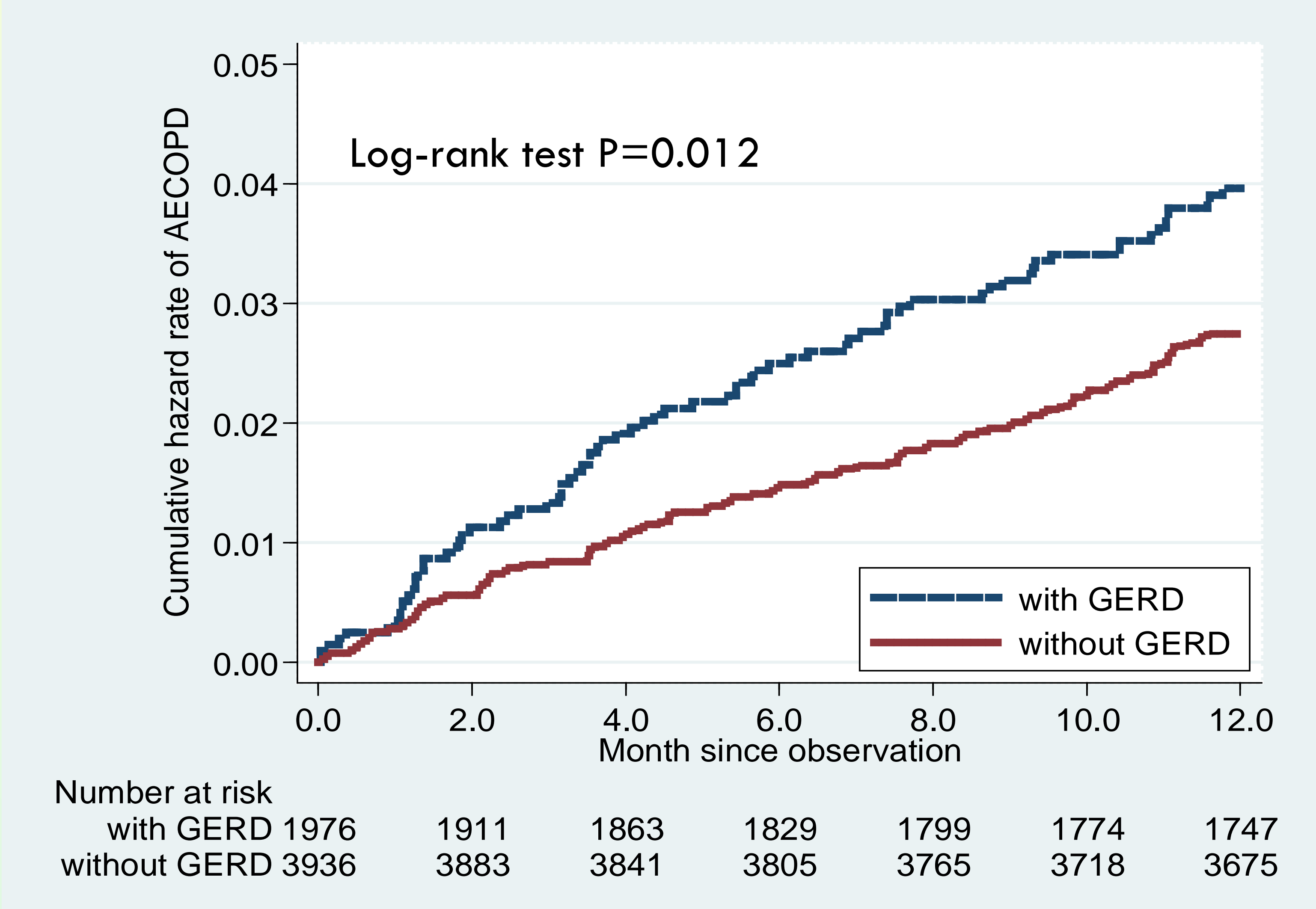
## Results

The baseline characteristics of the patients are shown in table 1. There was no significant difference between the two groups in terms of the prevalence of co-morbidities, COPD severity, socioeconomic status, or other covariates at baseline.

Table 1: Baseline Characteristic in COPD patients with and without GERD

Characteristic	With GERD (N=1976)	Without GERD (N=3936)	P Value
Male	1296 (65.59)	2591 (65.83)	0.854
Age (SD)	64.91 (± 12.26)	64.98 (± 12.11)	0.834
Comorbidities			
IHD	905 (45.80)	1772 (45.02)	0.570
HF	278 (14.07)	547 (13.9)	0.858
AF	84 (4.25)	174 (4.42)	0.763
Hypertension	1310 (66.30)	2614 (66.41)	0.928
Osteoporosis	394 (19.94)	744 (18.9)	0.340
Anxiety	581 (29.40)	1136 (28.86)	0.666
DM	605 (30.62)	1189 (30.21)	0.747
Angina	304 (15.38)	564 (14.33)	0.279
Stroke	565 (28.59)	1165 (29.6)	0.423
Anemia	267 (13.51)	536 (13.62)	0.911
Dementia	151 (7.64)	324 (8.23)	0.431
COPD medications			
SABA	267 (13.51)	474 (12.04)	0.108
LABA	13 (0.66)	41 (1.04)	0.143
SABA & SAMA	79 (4.0)	141 (3.58)	0.426
ICS	69 (3.49)	132 (3.35)	0.782
SAMA	241 (12.2)	413 (10.49)	0.050
LAMA	20 (1.01)	34 (0.86)	0.572
Theophylline	1675 (84.77)	3304 (83.94)	0.412
Vaccines			
Influenza	1109 (56.12)	2088 (53.05)	0.025
Pneumococcal	212 (10.73)	431 (10.95)	0.796
COPD severity	56 (2.83)	106 (2.69)	0.754
Residential area			
Urban	1074 (54.35)	2075 (52.72)	0.452
Suburban	690 (34.92)	1410 (35.82)	
Rural	212 (10.73)	451 (11.46)	
Occupation categories			
Category 1	639 (32.34)	1227 (31.17)	0.863
Category 2	756 (38.26)	1612 (40.96)	
Category 3	581 (29.40)	1097 (27.87)	
Monthly insurance premium (\$NT)			
No fee	697 (35.27)	1397 (35.49)	0.921
1~19199	559 (28.29)	1061 26.96)	
19200~23999	605 (30.62)	1274 (32.37)	
≥ 24000	115 (5.82)	204 (5.18)	
OPD visit times before index day			
0	702 (35.53)	1464 (37.2)	0.976
1~2	597 (30.21)	1055 (26.8)	
>3	677 (34.26)	1417 (36)	

Figure1: The difference in the cumulative incidence rate of AECOPD between COPD with GERD and without GERD within twelve months.



### Acute exacerbation of COPD patients with GERD

The main outcome of this study was the occurrence of an AECOPD event. Figure 1 presents a Kaplan-Meier curve illustrating the overall survival based on the cumulative incidence of AECOPD during the 12-month follow-up. The incidence of AECOPD was significantly higher in subjects with GERD (p =0.012). During the 12-month follow-up period, the cumulative incidence was 3.40 (95% CI, 2.71 – 4.26) per 1,000 person-months in COPD with GERD while 2.32 per 1,000 person-months (95% CI, 1.92–2.81) in non-GERD subjects. The unadjusted and adjusted hazard ratios for the parameters in this study were all included as potential covariates in the forward stepwise Cox regression model. The results demonstrate that COPD with a coexisting diagnosis of GERD was an independent prognostic variable ( $HR_{adj} = 1.48$ ; 95% CI, 1.10 ~ 1.99; P = 0.010) (Table 2).

Table 2. Hazard ratios and incidence rate per 1,000 person-month among COPD with GERD and without GERD within twelve months of follow-up period

Groups	Person-Month	AECOPD event	Rate	95% CI	P value
With GERD	22076.93	75	3.40	2.71 ~ 4.26	
Without GERD	45616.57	106	2.32	1.92 ~ 2.81	
Crude HR			1.45	1.08 ~ 1.96	0.012
*Adjusted HR			1.48	1.10 ~ 1.99	0.010

\*Adjusted for age, sex, IHD, HF, AF, HT, Osteroporosis, Anxiety, DM, Angina, Anemia, dementia, Number of OPD visit, COPD severity, Number of OPD visit, Occupation categories, Monthly insurance premium, Residential area.

## Conclusion

This study demonstrated that GERD is an independent risk factor for AECOPD. Caution should be exercised when assessing GERD symptoms in patients with COPD.

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